Reply to Office action of January 11, 2005

## Amendments to the Specification:

Please replace the first two paragraphs on page 14 with the following amended paragraphs:

For example, HeLa cell lines can be finely altered to, in one circumstance, over express the p53 protein, and in another circumstance to under express c-myc. These alterations involve the insertion of exogenous elements that enable the overproduction of a protein (knockin) or reduction in the production of a constitutive protein (knockdown) within the cell. Alternatively, the targeted gene can be prevented from expressing any protein (knockout) via a number of processes, including deletion of the gene or transcription promoting elements for the gene at the DNA level within the cell. Knockout modifications generally involve modification of the gene or genes within the genome (see, for example, Gonzalez (2001) "The use of gene knockout mice to unravel the mechanisms of toxicity and chemical carcinogenesis" Toxicol Lett 120:199 208). Knockdown modifications are typically achieved by either treatment with an exogenous agent (e.g. antisense or ribozyme) or by insertion into the genome of one or more vectors expressing a product that hybridizes to nucleic acid. The target nucleic acid is commonly RNA, although DNA molecules can also be targeted. Furthermore, knockouts can be either heterozygous (e.g. inactivating only one copy of the gene) or homozygous (inactivating both copies of the gene). One exemplary database of mouse knockouts can be found at http://research.bmn.com (the BioMedNet mouse knockout and mutation database).

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